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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/309,038	05/10/99	HEIFETZ	P A-30496B

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EXAMINER	
MEHTA, A	
ART UNIT	**PAPER NUMBER**
1638	11

DATE MAILED: 01/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/309,038	HEIFETZ ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) *41-44 and 71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-40,45-70 and 72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Specification

1. Lines 3-6 on page 1 of the specification indicate that the claims the benefit of a U.S. Provisional application, which was converted on from Application No. 09/084,942. However, the serial number of the provisional application is not provided. This number must be provided to claim the benefit of the earlier filing date.

Claim Objections

2. Claims 45 and 52 are objected to under 37 CFR 1.75 (b) as being duplicate claims. Both claims are drawn to a cell that contain the sense and antisense fragments of claim 1, and the cells of both claims can only be made by the broad method of claim 1. Applicant is required to cancel one of the claims, or amend the claim(s).

Likewise, claims 53-55 and 59-61 are also duplicate claims. The cells of claim 53 and 59 both comprise the DNA sequences of claim 12, and can only be made using the broad method of claim 12. Expression of "said target gene" would also be inhibited in the cell of claim 59, when the same DNA sequences are expressed. Applicant is required to cancel the claims, or amend the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-40, 45-70, and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations "capable of forming" in line 4 of claim 1, line 5 of claim 12, line 5 of claim 63, line 4 of claim 69, line 5 of claim 72, and "capable of folding" in line 1 of claims 11 and 23, render the claims and those dependent thereon indefinite. The recitation indicates that the double-stranded RNA molecule does not have to form. This makes the claimed invention unclear. For example, the method of claim 1 requires the expression of a viral genome to be altered. As described in the specification, the expression will not be altered unless the double-stranded molecule is formed. It is therefore not clear what the claims are drawn to if the duplex is not formed. To clarify the claimed invention and to be consistent with the specification, it is suggested that the claims be amended to indicate that a double-stranded RNA molecule does form.

4. Claims 46, 47, and 53-58 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "said target gene" in line 1 of claim 46 and line 2 of claim 53 render those claims, and dependent claims 47 and 54-58, indefinite. There is no previous mention of any target gene in claims 46 and 53, nor in the claims from which they depend.

5. Claim 62 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "the two DNA sequences of claim 8" renders the claim indefinite. Neither claim 8 nor any of the claims from which it depends include DNA sequences.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 63-70 and 72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey

to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any DNA construct comprising a first and second DNA sequence capable of expressing in any cell sense and antisense RNA fragments of a viral genome or portion thereof, or of any target gene, wherein said sense and antisense RNA fragments are capable of forming a double-stranded RNA molecule; further wherein expression of said viral genome or portion thereof, or said target gene, in said cell is altered.

The only DNA constructs described by the specification are those on pages 26-43. Other constructs are not described and not reduced to practice. The constructs described on pages 26-43 do not provide any structural or functional information of any other viral genome or portion thereof, or any other target gene. See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence), and at page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof. Also see Fiers vs. Sugarno, 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing any DNA construct comprising any first and second DNA sequences capable of expressing any sense or antisense RNA fragment, and lack of guidance as

discussed above, the specification fails to provide an adequate written description of the multitude of isolated DNA molecules encompassed by the claims.

7. Claims 1-40, 45-70, and 72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn towards a method comprising introducing into any cell a sense and antisense RNA fragment of any viral genome or portion thereof, wherein said sense and antisense fragments are capable of forming a double-stranded RNA molecule, wherein the expression of said viral genome in said cell is altered; or wherein a DNA sequences encoding said sense and antisense RNA fragments are introduced into said cell; the cell produced by said method.

The specification teaches the construction of plant transformation vectors comprising sense and/or antisense plant gene or plant viral genes (pages 41-43). However, the specification does not teach that the expression of any viral genome or target gene was altered in any way. The specification does not provide any explanation as to why this strategy of expressing both sense and antisense RNA fragments would be effective to render plant cells resistant or tolerant to viruses. At the time the application was filed, degradation of specific double-stranded RNA molecules was only speculated to be a possible mechanism of post-transcriptional gene silencing

(Stam et al, page 8). The instant specification does not demonstrate that the expression of the sense and antisense RNA molecules actually led to alteration of gene expression in cells. The teachings of the specification therefore do not further the speculation of the prior art. Therefore, in the absence of further guidance, or a declaration presenting data indicating that the expression of the vectors taught in the Examples actually caused inhibition of gene expression in cells, it is unpredictable from the teachings of the specification whether the claimed method can be used to alter the expression of viral genomes or any target gene.

It is also unpredictable that such a strategy would be effective to increase viral resistance in non-plant cells. The structure of plant viruses is quite different from non-plant viruses. For example, non-plant viruses do not have a movement protein. Without further guidance, it is not clear that the invention can be used to increase virus resistance of any cell. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the claims encompassing altering expression of any viral genome in any cell type, unpredictability of the art and lack of guidance of the specification, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

8. Claims 1-40, 45-70, and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting plant viral protein expression in plant cells, does

not reasonably provide enablement for any other type of alteration of expression of any viral genome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn towards a method comprising introducing into any cell a sense and antisense RNA fragment of any viral genome or portion thereof, wherein said sense and antisense fragments are capable of forming a double-stranded RNA molecule, wherein the expression of said viral genome in said cell is altered; or wherein a DNA sequences encoding said sense and antisense RNA fragments are introduced into said cell; the cell produced by said method.

The specification teaches a method to increase virus resistance of a plant cell, wherein the method involves expressing the sense and antisense RNA fragments from a viral genome in a host plant cell such that the fragments will form a double-stranded RNA molecule. The claims, however, broadly read on any king of alteration of expression of the viral genome. It is not clear how the method can alter viral genome expression other than to inhibit viral protein expression. That is, the claims broadly encompass an alteration in which expression is increased. The specification does not teach using the claimed method to increase the sensitivity of a cell to a virus. Waterhouse et al (Proc. Natl. Acad. Sci. USA, Vol. 95, November 1998) use the same strategy taught in the instant specification to induce virus resistance and viral gene silencing in plants, and show how that the silencing effect occurs via a post-transcriptional mechanism (pages

13960-13964). It is evident that the only alteration in the expression of the viral genome of the instant invention can be a silencing effect. It is suggested that the claims be amended to exclude alterations of viral genome expression in which expression is increased. Given the breadth of the claims encompassing an increase in expression of the viral genome, unpredictability of the art, and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 63, 65, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Krueger et al.

The claims are broadly drawn towards any DNA construct comprising first and second DNA sequences capable of expressing sense and antisense RNA fragments in a cell, wherein in said RNA fragments are capable of forming a double-stranded RNA molecule.

Krueger et al teach the double-stranded DNA genome of the Feldmannia sp. virus (pages 301-302). If expressed, sense and antisense RNA fragments of the genome would form. Since they are complementary, the sense and antisense RNA fragments would be capable of forming a double-stranded molecule. As claim 63 does not require promoters to be present in both DNA strands of the viral DNA genome, Krueger et al teaches the claimed invention.

10. Claims 1, 10, 11, 45, 46, and 52 are rejected under 35 U.S.C. 102(a) as being anticipated by Miles et al (U.S. Patent No. 5,738,985).

The claims are broadly drawn towards a method comprising introducing into any cell a sense and antisense RNA fragment of any viral genome or portion thereof, wherein said sense and antisense fragments are capable of forming a double-stranded RNA molecule, wherein the expression of said viral genome in said cell is altered; cells comprising said sense and antisense RNA fragments.

Miles et al teach infection of HeLa cells by the double-stranded RNA poliovirus (col. 36, line 51 to col. 37, line 5). As genes from the viral genome are expressed in HeLa cells, the expression of the viral genome can be said to be altered. As broadly claimed, the reference teaches the claimed invention.

CLOSING REMARKS

Any inquiry concerning this communication should be directed to Examiner Ashwin Mehta, whose telephone number is (703) 306-4540. The Examiner can normally be reached Monday-Thursday and alternate Fridays, from 8:00 A.M. - 5:30 P.M. The fax phone number for the group is (703) 305-3014. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. Any inquiry of a general nature or relating to the status of the application should be directed to the art unit's Patent Analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475.

Ashwin D. Mehta

January 16, 2001

GARY BENZION
PRIMARY EXAMINER